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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/591,986	09/07/2006	Ryuji Ueno	Q80545	9326
23373 7590 08/05/2010 SUGHRUE MION, PLLC 2100 PENNSYLVANIA AVENUE, N.W. SUITE 800 WASHINGTON, DC 20037				
EXAMINER THOMAS, TIMOTHY P				
ART UNIT		PAPER NUMBER		
1628				
NOTIFICATION DATE		DELIVERY MODE		
08/05/2010		ELECTRONIC		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary

Application No.

10/591,986

Applicant(s)

UENO ET AL.

Examiner

TIMOTHY P. THOMAS

Art Unit

1628

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 October 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-19 is/are pending in the application.
- 4a) Of the above claim(s) 1-19 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-10 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/C)
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date: _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____
- Paper No(s)/Mail Date: _____

DETAILED ACTION

Response to Arguments

1. Applicants' arguments, filed 10/8/2009, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

2. Applicant's request for rejoinder is noted. However, no rejoinder is made at this time, since the elected claims are not currently allowable.

3. Applicant's arguments with respect to the obviousness rejection have been fully considered but they are not persuasive:

Claims 1-10 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Inoue, et al. (WO 2004/067521 A1; priority date 2003 Jan 27; IDS 3/30/2007 reference) and Ogata et al. (US 4,780,465; 1988); in view of Niebergall ("Ionic Solutions and Electrolytic Equilibria"; 2000; "Remington: The Science and Practice of Pharmacy"; 20th Ed.; Gennaro, Ed.; Lippincott Williams & Wilkins; Chapter 17, pp. 227-245).

The rejection is maintained for the reasons of record.

Applicant argues that the teaching of Niebergall, that the aqueous solubility of a slightly soluble organic substance generally is affected markedly by the addition of an electrolyte, is not applicable to the compound of the instant invention; quotes from Niebergall are presented. Applicant further argues the term "slightly soluble" is defined in the attached General Notices part of the US Pharmacopeia to correspond to solubility

of 1mg/mL-10 mg/mL; based on the solubilities of compounds A, B, and C in the instant disclosure, Table 1, the solubilities fall within the slightly soluble range; that compounds A and C were precipitated (salted out) at the NaCl concentrations of 0.4 and 0.85% (0.068M and 0.14M, respectively), while compound B was not precipitated; this translates into the precipitation of compounds by a concentration of NaCl significantly lower than 0.5 M. Somehow this data is argued to demonstrate that Nievergall is not applicable to the compound of the instant claims.

Applicant further argues that Compound A, B and C are disclosed in Inoue; all of these compounds are "slightly soluble" compounds, but the effect of NaCl on the solubility of these compounds is different; that this is not suggested by Inoue; that accordingly the instant claims would not have been come up with by one of ordinary skill in the art based on the combination of Inoue and Niebergall.

This is not persuasive. Niebergall is a generally applicable reference that teaches the phenomenon of salting out. Niebergall discusses empirical relationships relating solubility of the organic substance in water, in electrolyte, the salt concentration and a constant (see equation 12, p. 231). As is usually expected in the art, while such empirical equations model behavior, constants typically vary from one organic compound to another, i.e. the value of K_s or K'_s (in equation 13) would be expected to vary a little from one compound to another compound, as is reflected by the data used in the arguments. The fact that one compound out of 3 did not salt out under the conditions tested does not demonstrate that salting out does not occur with this compound. To establish this point would require a measurement of solubility as a

function of salt concentration. Observation of differences in properties between different compounds is typical in the art; indeed, MPEP 716.02 indicates:

Any differences between the claimed invention and the prior art may be expected to result in some differences in properties. The issue is whether the properties differ to such an extent that the difference is really unexpected. *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

This reflects that different compounds are expected to have some differences in properties.

The salting out phenomena, taught by Niebergall, provides motivation to substitute an alternate isotonic compound, i.e., glycerin, mannitol or boric acid, instead of the alternate NaCl, taught by Ogata as isotonic agents. It also provides motivation to exclude NaCl, by selecting an alternate non-salt isotonic agent, giving the compositions of the instant claims, within the scope of the "consisting essentially of" claim amendment, which applicant has argued excludes NaCl, based on disclosed data from Tables 1 and 2. The teaching of Niebergall also establishes that the salting out is not somehow an unexpected result over the teachings of the prior art references.

The obviousness rationale is not somehow rebutted by differing amounts of NaCl that are recognized to precipitate the compound, even when they occur at lower values than Niebergall teaches, or the observation of salting out not being observed, under the conditions tested.

As was pointed out previously, there are no unexpected results on the record with respect to the elected compound, which is under examination, and is the basis for

the rejection. These arguments do not establish any unexpected result for the elected compound.

Conclusion

4. No claim is allowed.
5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **TIMOTHY P. THOMAS** whose telephone number is (571) 272-8994. The examiner can normally be reached on Monday-Thursday 6:30 a.m. - 5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Timothy P Thomas/
Examiner, Art Unit 1628